



FFW

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE  
Group Art Unit 1639

In re

Patent Application of

David Edwin Thurston, et al.

Application No. 10/602,521

Confirmation No.: 2183

Filed: June 24, 2003

Examiner: Unknown

“COLLECTION OF COMPOUNDS”

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT  
PURSUANT TO 37 CFR §1.97(b)

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

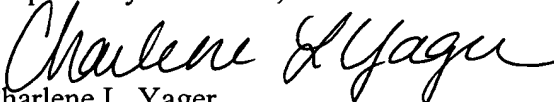
Sir:

The Examiner's attention is directed to the references which are listed on the attached Form PTO/SB/08A and PTO/SB/08B and copies of non-U.S. patent references are attached.

Citation of these references is respectfully requested.

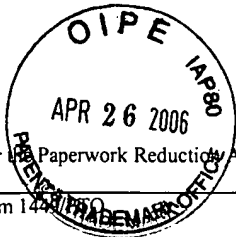
No concession is made that these documents are prior art, and Applicant expressly reserves the right to antedate the documents as may be appropriate.

Respectfully submitted,

  
Charlene L. Yager  
Reg. No. 48,887

File No. 065435-9027-US00

Michael Best & Friedrich LLP  
One South Pinckney Street  
P. O. Box 1806  
Madison, WI 53701-1806  
608.257.3501



<b>Substitute for form 1449</b> <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary) Sheet 1 of 2	<b>Complete if Known</b>	
	<b>Application Number</b>	10/602,521
	<b>Filing Date</b>	June 24, 2003
	<b>First named Inventor</b>	David Edwin Thurston
	<b>Group Art Unit</b>	1639
	<b>Examiner name</b>	Unknown
	<b>Attorney Docket Number</b>	065435-9027-US00

**U.S. Patent Documents**

Examiner Initials	U.S. Patent Document Number	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document
	6,660,856	Wang	12/9/2003

**FOREIGN PATENT DOCUMENTS**

Examiner Initials	Country Code	Foreign Patent Document Number	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document	Translation	English Abstract
	EP	1193270	Spirogen Ltd.	4/3/2002		
	GB	2053894	The Green Cross Corporation	2/11/1981		
	WO	88/04659	The Upjohn Company	6/30/1988		
	WO	91/16324	The Upjohn Company	10/31/1991		
	WO	96/23497	Synphar Laboratories, Inc.	8/8/1996		
	WO	97/07097	Auckland Division Cancer Society of New Zealand Inc.	2/27/1997		
	WO	98/11101	Auckland Division Cancer Society of New Zealand Inc.	3/19/1998		
	WO	98/12197	Kyorin Pharmaceuticals Co., Ltd. et al.	3/26/1998	N	Y
	WO	99/29642	The Scripps Research Institute	6/17/1999		
	WO	99/46244	Novo Nordisk A/S et al.	9/16/1999		

<b>Examiner Signature</b>		<b>Date Considered</b>	
-------------------------------	--	----------------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

**Burden Hour Statement:** This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer. Patent and Trademark Office, Washington, DC 0231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB control number.

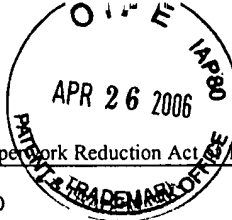
<b>Substitute for form 1449/PTO</b>  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)  Sheet 2 of 2				<b>Complete if Known</b>			
				Application Number		10/602,521	
				Filing Date		June 24, 2003	
				First named Inventor		David Edwin Thurston	
				Group Art Unit		1639	
				Examiner name		Unknown	
				Attorney Docket Number		065435-9027-US00	
<b>U.S. Patent Documents</b>							
<b>FOREIGN PATENT DOCUMENTS</b>							
Examiner Initials	Country Code	Foreign Patent Document Number	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document	Translation	English Abstract	
	WO	00/12508	The University of Portsmouth Higher Education Corp.	3/9/2000			
	WO	00/12509	The University of Portsmouth Higher Education Corp.	3/9/2000			
	WO	00/64864	Cancer Campaign Research Technology Ltd.	11/2/2000			
	WO	2004/043963	Spirogen Ltd.	5/27/2004			
	WO	2005/023814	Spirogen Ltd.	3/17/2005			
	WO	2005/040170	Government of the U.S.A. et al.	5/6/2005			
	WO	2005/085251	Spirogen Ltd.	9/15/2005			

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer. Patent and Trademark Office, Washington, DC 0231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box Alexandria, VA 22313-1450.



Substitute for form 1449B/PTO

**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

(use as many sheets as necessary)

**Complete if Known**

Application Number	10/602,521
Filing Date	June 24, 2003
First Named Inventor	David Edwin Thurston
Group Art Unit	1639
Examiner Name	Unknown
Attorney Docket Number	065435-9027-US00

Sheet 1 of 5

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc. ), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
		ADAMS et al., "Molecular modelling of a sequence-specific DNA-binding agent based on the pyrrolo[2,1-c][1,4]benzodiazepines," Pharm. Pharmacol. Commun. (1999) 5:555-560
		BARALDI, P.G. et al., "[2,1-c][1,4]benzodiazepine (PBD)-distamycin hybrid inhibits DNA binding to transcription factor Sp1," Nucleotides and Nucleic Acids (2000) 19(8):1219-1229
		BERGÈ et al., "Pharmaceutical Salts," J. Pharm. Sci. (1977) 66:1-19
		BORGATTI, M. et al., "Inhibition of NF-kB/DNA interactions and HIV-1 LTR directed transcription by hybrid molecules containing pyrrolo [2,1-c][1,4] benzodiazepine (PBD) and oligopyrrole carriers," Drug Development Research (2003) 60(3):173-185
		BOSE, D.S. et al., "Effect of linker length on DNA-binding affinity, cross-linking efficiency and cytotoxicity of C8 linked pyrrolobenzodiazepine dimers," J. Chem. Soc. Chem. Commun. (1992) 20:1518-1520
		CHEN, Z. et al., "A novel approach to the synthesis of cytotoxic C2-C3 unsaturated pyrrolo[2,1-c][1,4]benzodiazepines (PBDs) with conjugated acrylyl C2-substituents," Biorg. Med. Chem. Lett. (2004) 14:1547-1549
		COOPER, N. et al., "Synthesis of novel PBDs as anti-tumour agents," Chem. Commun. (2002) 16:1764-1765
		DE GROOT, FMH et al., "Synthesis and biological evaluation of 2'-carbamate-linked 2'-carbonate-linked prodrugs of paclitaxel: selective activation by the tumor-associated protease plasmin," J. Med. Chem. (2000) 43(16):3093-3102
		DE GROOT, FMH et al., "Novel 20-carbonate linked prodrugs of camptothecin and 9-aminocamptothecin designed for activation by tumour-associated plasmin," Biorg. Med. Chem. Lett. (2002) 12(17):2371-2376

**Examiner  
Signature****Date  
Considered**

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB number.

Substitute for form 1449B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/602,521
				Filing Date	June 24, 2003
				First Named Inventor	David Edwin Thurston
				Group Art Unit	1639
				Examiner Name	Unknown
Sheet	2	of	5	Attorney Docket Number	065435-9027-US00

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc. ), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
		DUBOWCHIK, G.M. et al., "Cathepsin B-sensitive dipeptide prodrugs. 1. A model study of structural requirements for efficient release of doxorubicin," Biorg. Med. Chem. Lett. (1998) 8:3341-3346
		DUBOWCHIK, G.M. et al., "Cathepsin B-sensitive dipeptide prodrugs. 2. Models of anticancer drugs paclitaxel (Taxol), Mitomycin C and Doxorubicin," Biorg. Med. Chem. Lett. (1998) 8:3347-3352
		DUBOWCHIK and WALKER, "Receptor-mediated and enzyme-dependent targeting of cytotoxic anticancer drugs," Pharmacology and Therapeutics (1999) 83:67-123
		GARSKY et al., "The synthesis of a prodrug of doxorubicin designed to provide reduced systemic toxicity and greater target efficacy," J. Med. Chem. (2001) 44:4216-4224
		GREGSON, S.J. et al., "Effect of C2/C3-endo unsaturation on the cytotoxicity and DNA-binding reactivity of pyrrolo-[2,1-c][1,4]-benzodiazepines," Bioorg. Med. Chem. Lett. (2000) 10(16):1849-1851
		GREGSON, S.J. et al., "Linker length modulates DNA cross-linking reactivity and cytotoxic potency of C8/C8' ether-linked C2-exo-unsaturated pyrrolo[2,1-c][1,4]benzodiazepine (PBD) dimers," J. Med. Chem. (2004) 1161-1174
		GREGSON, S.J. et al., "Synthesis of the first example of a C2-C3/C2'-C3'-endo unsaturated pyrrolo[2,1-c][1,4]benzodiazepine dimer," Biorg. Med. Chem. Lett. (2001) 11:2859-2862
		GREGSON, S.J. et al., "Synthesis of the first examples of A-C8/C-C2 amide-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers," Biorg. Med. Chem. Lett. (2003) 13:2277-2280
		HAMBURGER, A.W. et al., "Primary bioassay of human tumor stem cells," Science (1977) 197:461-643

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB number.

Substitute for form 1449B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/602,521
				Filing Date	June 24, 2003
				First Named Inventor	David Edwin Thurston
				Group Art Unit	1639
				Examiner Name	Unknown
Sheet	3	of	5	Attorney Docket Number	065435-9027-US00

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc. ), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
		JAKOBSEN et al., "Design, synthesis, and pharmacological evaluation of thapsigargin analogues for targeting apoptosis to prostatic cancer cells," J. Med. Chem. (2001) 44:4696-4703
		KAMAL et al., "Synthesis and DNA-binding affinity of A-C8/C-C2 alkoxyamido-linked pyrrolo[2,1-c][1,4]benzodiazepine dimers" Biorg. Med. Chem. Lett. (2003) 13(22):3955-3958
		KAMAL, et al., "Synthesis of pyrrolo[2,1-c][1,4]benzodiazepines via reductive cyclization of w-azido carbonyl compounds by TMSI: an efficient preparation of antibiotic DC-81 and its dimers," Biorg. Med. Chem. Lett. (2000) 10:2311-2313
		KANEKO, T. et al., "Bicyclic and tricyclic analogues of anthramycin," J. Med. Chem. (1985) 28:388-392
		KANG, G.-D. et al., "Synthesis of a novel C2-aryl substituted 1,2-unsaturated pyrrolobenzodiazepine," Chem. Commun. (2003) 1688-1689
		KUMAR, R. et al., "Synthesis and antitumor cytotoxicity evaluation of novel pyrrolo[2,1-c][1,4]benzodiazepine imidazole containing polyamide conjugates," Oncology Research (2003) 13(4):221-223
		KUMAR, R. et al., "Design and synthesis of novel pyrrolo[2,1-c][1,4]benzodiazepine - imidazole containing polyamide conjugates," Heterocyclic Communications (2002) 81(1):19-26
		KUMAR, R. et al., "Design, synthesis and in vitro cytotoxicity studies of novel pyrrolo [2,1][1,4]benzodiazepine-glycosylated pyrrole and imidazole polyamide conjugates," Org. Biomol. Chem. (2003) 1(19):3327-3342
		LANGLOIS, N. et al., "Synthesis and cytotoxicity on sensitive and doxorubicin-resistant cell lines of new pyrrolo[2,1-c][1,4]benzodiazepines related to anthramycin," J. Med. Chem. (2001) 44:3754-3757

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB number.

Substitute for form 1449B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/602,521
				Filing Date	June 24, 2003
				First Named Inventor	David Edwin Thurston
				Group Art Unit	1639
				Examiner Name	Unknown
Sheet	4	of	5	Attorney Docket Number	065435-9027-US00

**OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS**

Examiner Initials		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc. ), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
		LIPSHUTZ, B.H. et al., "Pd(II)_Catalyzed Acetal/Ehtal Hydrolysis/Exchange Reactions," Tetrahedron Lett. (1985) 26(6):705-708
		MHAKA et al., "A 5-fluorodeoxyuridine prodrug as targeted therapy for prostate cancer," Biorg. Med. Chem. Lett. (2002) 12(17):2459-2461
		MISCHIATI, C. et al., "Binding of hybrid molecules containing pyrrolo [2,1-c][1,4]benzodiazepine (PBD) and oligopyrrole carriers to the human immunodeficiency type 1 virus TAR-RNA," Biochem. Pharmacol. (2004) 67(3):401-410
		MORI, M. et al., "Total syntheses of prothracarcin and tomaymycin by use of palladium catalyzed carbonylation," Tetrahedron (1986) 42(14):3793-3806
		MOUNTZOURIS, J.A. et al., "Comparison of a DSB-120 DNA interstrand cross-linked adduct with the corresponding bis-Tomamycin adduct," J. Med. Chem. (1994) 37:3132-3140
		NICULESCU-DUVAZ, D. et al., "Self-immolative nitrogen mustard prodrugs for suicide gene therapy," J. Med. Chem. (1998) 41(26):5297-5309
		REDDY et al., "Design, synthesis and in vitro cytotoxicity studies of novel pyrrolo[2,1-c][1,4]benzodiazepine (PBD)-polyamide conjugates and 2,2'-PBD dimers," Anti-Cancer Drug Design (2000) 15(3):225-228
		SPELLIE, M. et al., "Cellular pharmacology of novel C8-linked anthramycin-based sequence-selective DNA minor groove cross-linking agents," Br. J. Cancer (1994) 70:48-53
		SPELLIE, M. et al., "Sequence selective recognition of duplex DNA through covalent interstrand cross-linking," Biochem. (2003) 42:8232-8239

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231.  
DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB number.

Substitute for form 1449B/PTO  <b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)				<b>Complete if Known</b>	
				Application Number	10/602,521
				Filing Date	June 24, 2003
				First Named Inventor	David Edwin Thurston
				Group Art Unit	1639
				Examiner Name	Unknown
Sheet	5	of	5	Attorney Docket Number	065435-9027-US00

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS		
Examiner Initials		Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc. ), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
		THURSTON, D.E., "Nucleic acid targeting: therapeutic strategies for the 21st century," Brit. J. Cancer (1999) 80(1):65-85
		TIBERGHEN, A.C. et al., "Application of the stille coupling reaction to the synthesis of C2-substituted endo-exo unsaturated pyrrolo[2,1-c][1,4]benzodiazepines (PBDs)," Biorg. Med. Chem. Lett. (2004) 14:5041-5044
		WELLS, G. et al., "Pyrrolobenzodiazepine-polyamide libraries: synthesis and DNA binding selectivity," Proc. Am. Assoc. Canc. Res. (2003) 44:85-86, #452
		WERMUTH et al., "Molecular Variations Based on Isosteric Replacements," The Practice of Medicinal Chemistry, Chapter 13 (1996) 203-237
		WILLIAMS, M.A. et al., "Synthesis of conformationally constrained DTPA analogues. Incorporation of the ethylenediamine units as aminopyrrolidines," J. Org. Chem. (1994) 59(13):3616-3625

Examiner Signature		Date Considered	
-----------------------	--	--------------------	--

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer, Patent and Trademark Office, Washington, DC 20231.  
DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.